# 1/48

# http://www.ncbi.nlm.nih.gov/entrez 1: AY207429. Homo sapiens inte...[gi:27501935]

Links

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SOURCE							
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		i; Metazoa; Che	ruaca, oru	i.zaca,	.020022	•	
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	Mammalia	1 to 9803)	inaces, cac	~~~	,		
REFERENCE	1 (bases	.J., Carrington	ch an	Ponte S	H. Hasti	inas.N.	C.,
AUTHORS	Rieder, M	.O., Kuldanek,	n, D. F., da e B Deikn	mar N	Toth.E.J.	Yi.C	and
	Anearn, M	.O., Kuldanek,	טיערטע יישיפי		100,210	.,,	
	Nickerson						
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51 ADTRQLAAQL LRRAGGSSLK IRAAHAILGG	10:2- : 51 EDTRQLTIQL LRRAMGSSLK IRAAHAILGG	51 ADTRQLAAQM LRRAGGPSLK IRAAHAILGG	: 51 ADTRQLAAQM LRRAAGPSLK IRAAHAILGG
41 STVLLTRSLL LLSYLRHVQW LAPPSSAWGG	macaque IL-11 (Macaca fascicularis) -SEQ ID NO:2-: 11 21 31 41 51 7 VISIMPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL 1 NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK 2 TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG	us) -SEQ ID NO:3-: 31 41 51 VSSDPRADLD SAVLLTRSLL ADTRQLAAQM PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK QAAPDQPVIP LGPPASAWGS IRAAHAILGG	gicus) -SEQ ID NO:4-:31 VSSDPRADLD SAVLLTRSLL PGVLTRLRVD LMSYFRHVQW QAAPDQPAVP LGPPASAWGS
:1-: 31 VSPDPRAELD PGVLTRLRAD QPPPDPPAPP	fascicularis 31 ASPDPRAELD PSVLTRLRAD QLPPDPPAPP	(Mus musculus) -SEQ ID NO:3-21 31 41 APGPPAGSPR VSSDPRADLD SAVLLT SAGTLGSLQL PGVLTRLRVD LMSYLR QLLMSRLALP QAAPDQPVIP LGPPAS	
-SEQ ID NO:1-:	11 (Macaca f		Rattus norve
21	21		21
APGPPPGPPR VSP	APGPPGSPR		7 APGPPAGSPR
SAGALGALQL PGV	SAGALGALQL		1 SAGTLGSLQL
QLLMSRLALP QPP	QLIMSRLALP		1 QLLMSRLALP
human IL-11 11 VLSIWPDTAV NLDSLPTLAM ARLDRLIRRL	macaque IL-1 11 'VLSIWPDTAV 'NLDSLPTLAM 'TRLDRLLRRL'	mouse IL-11 11 7 VLSIWPDRVV SLDSLPTLAM ARLERLLRRL RGLLLKTRL	rat IL-11 (R 11 / VLSLWPDRVV H NLDSLPTLAM D ARLERLLRRL R GLLLKTRL
Complete native 1	Complete native :  1 1 MNCVCRLVLV 61 KDKFPADGDH 121 TLEPELGTLQ	Complete native 1	Complete native 1
1 NNCVCRLVLV		1 NNCVCRLVLV	1 1 MNCVCRLVLV
61 RDKFPADGDH		61 RDKFPADGDH	61 RDKFPADGDH
121 TLEPELGTLQ		121 TLEPELGALQ	121 TLEPELGALQ
181 LHLTLDWAVR		181 LHLTLDWAVR	181 LHLTLDWAVR
Com	Com	Con	Con
1	1	1	

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## Native human IL-11 deleted from the 34 first aminoacids -SEQ ID NO :5-:

PRAELD STVLLTRSLL ADTRQLAAQL RDKFPADGDH NLDSLPTLAM SAGALGALQL PGVLTRLRAD LLSYLRHVQW LRRAGGSSLK TLEPELGTLQ ARLDRLLRRL QLLMSRLALP QPPPDPPAPP LAPPSSAWGG IRAAHAILGG LHLTLDWAVR GLLLLKTRL

## Native macaque IL-11 deleted from the 34 first aminoacids -SEQ ID NO:6-:

PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG L<u>H</u>LTL<u>D</u>WAVR GLLLLKTRL

#### Native mouse IL-11 deleted from the 34 first aminoacids -SEQ ID NO:7-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>H</u>LTL<u>D</u>WAVR GLLLLKTRL

# Native rat IL-11 deleted from the 34 first aminoacids -SEQ ID NO:8-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LHLTLDWAVR GLLLLKTRL

#### 11/48

## hIL-11 mutein deriving from 34aa-deleted native human hIL-11 -SEQ ID NO :9-:

PRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSLPTLAMSAGALGA LQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGTLQARLDRLLRRL QLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGLX1LTLX2WAVRGLL LLKTRL wherein X1 and X2 are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

# hIL-11 mutein deriving from 34aa-deleted native human hIL-11 -SEQ ID NO :10-:

PRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSLPTLAMSAGALGA LQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGTLQARLDRLLRRL QLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>V</u>LTL<u>A</u>WAVRGLLL LKTRL

hIL-11 mutein deriving from 34aa-deleted native human hIL-11 -SEQ ID NO :11-:

PRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSLPTLAMSAGALGA LQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGTLQARLDRLLRRL QLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>A</u>LTL<u>V</u>WAVRGLLL

hIL-11 mutein deriving from 34aa-deleted native human hIL-11 -SEQ ID NO :12-:

PRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSLPTLAMSAGALGA LQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGTLQARLDRLLRRL QLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>V</u>LTL<u>V</u>WAVRGLLL LKTRL

hIL-11 mutein deriving from 34aa-deleted native human hIL-11 -SEQ ID NO :13-:

PRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSLPTLAMSAGALGA LQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGTLQARLDRLLRRL QLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>A</u>LTL<u>A</u>WAVRGLLL LKTRL

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# hIL-11 mutein deriving from 21aa-deleted native human hIL-11 -SEQ ID NO :14-:

PGPPPGPPRVSPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSL PTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGT LQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGLX1 LTLX2WAVRGLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

## hIL-11 mutein deriving from 21aa-deleted native human hIL-11 -SEQ ID NO :15-:

PGPPPGPPRVSPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSL PTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGT LQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>V</u>L TL<u>A</u>WAVRGLLLLKTRL

# hIL-11 mutein deriving from 21aa-deleted native human hIL-11 -SEQ ID NO :16-:

PGPPPGPPRVSPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSL PTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGT LQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>A</u>L TLVWAVRGLLLLKTRL

# hIL-11 mutein deriving from 21aa-deleted native human hIL-11 -SEQ ID NO :17-:

PGPPPGPPRVSPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSL PTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGT LQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL $\underline{\mathbf{V}}$ L TL $\underline{\mathbf{V}}$ WAVRGLLLLKTRL

# hIL-11 mutein deriving from 21aa-deleted native human hIL-11 -SEQ ID NO :18-:

PGPPPGPPRVSPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPADGDHNLDSL PTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSSLKTLEPELGT LQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRAAHAILGGL<u>A</u>L TLAWAVRGLLLLKTRL

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## hIL-11 mutein deriving from complete native human hIL-11 -SEQ ID NO :19-:

MNCVCRLVLVVLSLWPDTAVAPGPPPGPPRVSPDPRAELDSTVLLTRSLLADTR QLAAQLRDKFPADGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSLKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPL APPSSAWGGIRAAHAILGGLX1LTLX2WAVRGLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

## hIL-11 mutein deriving from complete native human hIL-11 -SEQ ID NO :20-:

MNCVCRLVLVVLSLWPDTAVAPGPPPGPPRVSPDPRAELDSTVLLTRSLLADTR QLAAQLRDKFPADGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSLKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPL APPSSAWGGIRAAHAILGGL<u>V</u>LTL<u>A</u>WAVRGLLLLKTRL

# hIL-11 mutein deriving from complete native human hIL-11 -SEQ ID NO :21-:

MNCVCRLVLVVLSLWPDTAVAPGPPPGPPRVSPDPRAELDSTVLLTRSLLADTR QLAAQLRDKFPADGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSLKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPL APPSSAWGGIRAAHAILGGL<u>A</u>LTL<u>V</u>WAVRGLLLLKTRL

## hIL-11 mutein deriving from complete native human hIL-11 -SEQ ID NO :22-:

MNCVCRLVLVVLSLWPDTAVAPGPPPGPPRVSPDPRAELDSTVLLTRSLLADTR QLAAQLRDKFPADGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSLKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPL APPSSAWGGIRAAHAILGGL<u>V</u>LTL<u>V</u>WAVRGLLLLKTRL

#### hIL-11 mutein deriving from complete native human hIL-11 -SEQ ID NO :23-:

MNCVCRLVLVVLSLWPDTAVAPGPPPGPPRVSPDPRAELDSTVLLTRSLLADTR QLAAQLRDKFPADGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSLKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPL APPSSAWGGIRAAHAILGGL<u>A</u>LTL<u>A</u>WAVRGLLLLKTRL

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# IL-11 mutein deriving from 34aa-deleted native macaque IL-11 -SEQ ID NO:24-:

PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LX1LTLX2WAVR GLLLLKTRL wherein X1 and X2 are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

IL-11 mutein deriving from 34aa-deleted native macaque IL-11 -SEQ ID NO:25-:
PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM
SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ
TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG
IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

IL-11 mutein deriving from 34aa-deleted native macaque IL-11 -SEQ ID NO:26-:
PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM
SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ
TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG
IRAAHAILGG LALTLWWAVR GLLLLKTRL

IL-11 mutein deriving from 34aa-deleted native macaque IL-11 -SEQ ID NO:27-:
PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM
SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ
TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG
IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

IL-11 mutein deriving from 34aa-deleted native macaque IL-11 -SEQ ID NO:28-:

PRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM
SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ
TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG
IRAAHAILGG LALTLAWAVR GLLLLKTRL

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# IL-11 mutein deriving from 21aa-deleted native macaque IL-11 -SEQ ID NO:29-:

PGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LX1LTLX2WAVR GLLLLKTRL wherein X1 and X2 are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I).
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

IL-11 mutein deriving from 21aa-deleted native macaque IL-11 -SEQ ID NO:30-:
PGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH
NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK
TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP
LAPPSSTWGG IRAAHAILGG LYLTLAWAVR GLLLLKTRL

IL-11 mutein deriving from 21aa-deleted native macaque IL-11 -SEQ ID NO:31-:
PGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH
NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK
TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP
LAPPSSTWGG IRAAHAILGG LALTLWWAVR GLLLLKTRL

IL-11 mutein deriving from 21aa-deleted native macaque IL-11 -SEQ ID NO:32-: PGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

IL-11 mutein deriving from 21aa-deleted native macaque IL-11 -SEQ ID NO:33-:
PGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH
NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK
TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP
LAPPSSTWGG IRAAHAILGG LALTLAWAVR GLLLLKTRL

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# IL-11 mutein deriving from complete native macaque IL-11 -SEQ ID NO:34-:

MNCVCRLVLV VLSLWPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LX1LTLX2WAVR GLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

IL-11 mutein deriving from complete native macaque IL-11 -SEQ ID NO:35-:

MNCVCRLVLV VLSLWPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL
EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD
LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP
QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LYLTLAWAVR GLLLLKTRL

IL-11 mutein deriving from complete native macaque IL-11 -SEQ ID NO:36-:

MNCVCRLVLV VLSLWPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL
EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD
LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP
QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LALTLYWAVR GLLLLKTRL

IL-11 mutein deriving from complete native macaque IL-11 -SEQ ID NO:37-:

MNCVCRLVLV VLSLWPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL
EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD
LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP
OLPPDPPAPP LAPPSSTWGG IRAAHAILGG LYLTLYWAVR GLLLLKTRL

IL-11 mutein deriving from complete native macaque IL-11 -SEQ ID NO:38-:

MNCVCRLVLV VLSLWPDTAV APGPPPGSPR ASPDPRAELD STVLLTRSLL
EDTRQLTIQL KDKFPADGDH NLDSLPTLAM SAGALGALQL PSVLTRLRAD
LLSYLRHVQW LRRAMGSSLK TLEPELGTLQ TRLDRLLRRL QLLMSRLALP
QLPPDPPAPP LAPPSSTWGG IRAAHAILGG LALTLAWAVR GLLLLKTRL

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#### IL-11 mutein deriving from 34aa-deleted native mouse IL-11 -SEQ ID NO:39-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LXILTLXWAVR GLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

#### IL-11 mutein deriving from 34aa-deleted native mouse IL-11 -SEQ ID NO:40-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

#### IL-11 mutein deriving from 34aa-deleted native mouse IL-11 -SEQ ID NO:41-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LALTLYWAVR GLLLLKTRL

## IL-11 mutein deriving from 34aa-deleted native mouse IL-11 -SEQ ID NO:42-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

#### IL-11 mutein deriving from 34aa-deleted native mouse IL-11 -SEQ ID NO:43-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>A</u>LTL<u>A</u>WAVR GLLLLKTRL

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# IL-11 mutein deriving from 21aa-deleted native mouse IL-11 -SEQ ID NO:44-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LX1LTLX2WAVR GLLLLKTRL wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P).
- Tryptophan (W).

# IL-11 mutein deriving from 21aa-deleted native mouse IL-11 -SEQ ID NO:45-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

# IL-11 mutein deriving from 21aa-deleted native mouse IL-11 -SEQ ID NO:46-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LALTLYWAVR GLLLLKTRL

# IL-11 mutein deriving from 21aa-deleted native mouse IL-11 -SEQ ID NO:47-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

# IL-11 mutein deriving from 21aa-deleted native mouse IL-11 -SEQ ID NO:48-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LALTLAWAVR GLLLLKTRL

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# IL-11 mutein deriving from complete native mouse IL-11 -SEQ ID NO:49-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LXLTLX2WAVR GLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

#### IL-11 mutein deriving from complete native mouse IL-11 -SEQ ID NO:50-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

#### IL-11 mutein deriving from complete native mouse IL-11 -SEQ ID NO:51-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LALTLVWAVR GLLLLKTRL

#### IL-11 mutein deriving from complete native mouse IL-11 -SEQ ID NO:52-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

## IL-11 mutein deriving from complete native mouse IL-11 -SEQ ID NO:53-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH SLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYLRHVQW LRRAGGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPVIP LGPPASAWGS IRAAHAILGG LALTLAWAVR GLLLLKTRL

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## IL-11 mutein deriving from 34aa-deleted native rat IL-11 -SEQ ID NO:54-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LX,LTLX,WAVR GLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

## IL-11 mutein deriving from 34aa-deleted native rat IL-11 -SEQ ID NO:55-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LVLTLAWAVR GLLLLKTRL

# IL-11 mutein deriving from 34aa-deleted native rat IL-11 -SEQ ID NO:56-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LALTLYWAVR GLLLLKTRL

# IL-11 mutein deriving from 34aa-deleted native rat IL-11 -SEQ ID NO:57-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

#### IL-11 mutein deriving from 34aa-deleted native rat IL-11 -SEQ ID NO:58-:

PRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LALTLAWAVR GLLLLKTRL

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## IL-11 mutein deriving from 21aa-deleted native rat IL-11 -SEQ ID NO:59-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LX,LTLX,WAVR GLLLLKTRL

wherein  $X_1$  and  $X_2$  are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

## IL-11 mutein deriving from 21aa-deleted native rat IL-11 -SEQ ID NO:60-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

#### IL-11 mutein deriving from 21aa-deleted native rat IL-11 -SEQ ID NO:61-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LALTLYWAVR GLLLLKTRL

# IL-11 mutein deriving from 21aa-deleted native rat IL-11 -SEQ ID NO:62-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LVLTLVWAVR GLLLLKTRL

# IL-11 mutein deriving from 21aa-deleted native rat IL-11 -SEQ ID NO:63-:

PGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LALTLAWAVR GLLLLKTRL

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# IL-11 mutein deriving from complete native rat IL-11 -SEQ ID NO:64-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LXLTLX2WAVR GLLLLKTRL wherein X1 and X2 are chosen from the group comprising:

- Alanine (A),
- Valine (V),
- Leucine (L),
- Isoleucine (I),
- Phenylalanine (F),
- Methionine (M),
- Proline (P),
- Tryptophan (W).

# IL-11 mutein deriving from complete native rat IL-11 -SEQ ID NO:65-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>A</u>WAVR GLLLLKTRL

# IL-11 mutein deriving from complete native rat IL-11 -SEQ ID NO:66-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG L<u>A</u>LTL<u>V</u>WAVR GLLLLKTRL

# IL-11 mutein deriving from complete native rat IL-11 -SEQ ID NO:67-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG L<u>V</u>LTL<u>V</u>WAVR GLLLLKTRL

# IL-11 mutein deriving from complete native rat IL-11 -SEQ ID NO:68-:

MNCVCRLVLV VLSLWPDRVV APGPPAGSPR VSSDPRADLD SAVLLTRSLL ADTRQLAAQM RDKFPADGDH NLDSLPTLAM SAGTLGSLQL PGVLTRLRVD LMSYFRHVQW LRRAAGPSLK TLEPELGALQ ARLERLLRRL QLLMSRLALP QAAPDQPAVP LGPPASAWGS IRAAHAILGG LALTLAWAVR GLLLLKTRL

# Joined CDS for human complete native IL-11 -SEQ ID NO:69-:

# Joined CDS for the IL-11 mutein which derives from the 34aa-deleted human IL-11 – SEO ID NO:70-:

wherein the codon  $n_1n_2n_3$  and the codon  $n_4n_5n_6$  are both chosen among the group comprising the nucleotide codons which codes for a hydrophobic aminoacid, namely for Alanine (A), Valine (V), Leucine (L), Isoleucine (I), Phenylalanine (F), Methionine (M), Proline (P), Tryptophan (W).

 $n_1n_2n_3$  and  $n_4n_5n_6$  can be chosen among the group comprising the following nucleotide codons:

- GCT, GCC, GCA, GCG
- GTT, GTC, GTA, GTG,
- TTA, TTG, CTT, CTC, CTA, CTG,
- ATT, ATC, ATA,
- TTT, TTC,
- ATG,
- CCT, CCC, CCA, CCG,
- TGG.

#### FIGURE 16A

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Joined CDS for the IL-11 mutein which derives from the 21aa-deleted human IL-11 - SEQ ID NO:71-:

wherein the codon  $n_1n_2n_3$  and the codon  $n_4n_5n_6$  are as defined in Figure 16A.

# Joined CDS for the IL-11 mutein which derives from the complete human IL-11 -SEQ ID NO:72-:

wherein the codon n<sub>1</sub>n<sub>2</sub>n<sub>3</sub> and the codon n<sub>4</sub>n<sub>5</sub>n<sub>6</sub> are as defined in Figure 16A.

#### FIGURE 16B

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#### Mutated AY207429 nucleic acid -SEQ ID NO:74-:

```
1 acacctgtat tcccaccact ttgggagget gaggcgggag gatgacctga getcaggagt
 61 ttgagaccag cctgggcaac atggcaaaac cctatctcta ctaaaaatac aaaaaatagc
121 caggcatggt ggcgggtgcc tgtaatccca gctactcagg aggctgaggc atgagaatca
181 cttgaacctg ggaggcggag gttacagtga gctgagatca caccactgca ccccagcctg
241 ggtgacacag cgagactetg teteaaaaaa accaaaaacg aggeeaggea eggtagetea
301 cacctgtcat cccagcactt tgggaggccg aggcaggcgg atcacgaagt caggagttcg
361 agaccagect ggccaacatg gtaagacece gtetetaeta aaaatacaaa attageeggg
421 tgtggtggcg cacacctgta atcccagcta cttgggaggc tgaggcagga gaatcgcttg
481 aaccegggag gtggaggttg cagtgagctg agattgtgcc attgatcgcg ccattgcact
541 ccagcctggg tgacagagtg agactcagta ccaaaaaaca aacaaacaaa aaacaaacaa
601 aaaatgagaa aggettttae tetetgeece cattgetgag teeceaacat eteagegtet
661 ctgtctttct aatatctctg tctccccttt tctgtccctg gggcctctcc gtccctgtca
721 ctctgccccg tgtctctgtt tgcctggtgc ctttcttcag ctgcggcatc ctctgtctca
781 gagtettggt gtetetgtte ettteecete ggggtetece tgggtetece caagteeete
841 etgetgtett cetecegete tetgatetet gacteceaga acetetecet etgtetecag
901 ggctgcccct ctgatcctct ttgcttctct ggtgtgtctc tctggctgcc tccatctctg
961 tggatctccg tctccctgtc tctgtctcag tctgtccttc actctgtgtg tgtgtgtgt
1021 tetetetete tetetetete ettecettee actecetett ectecigeet ceaectetee
1081 aggeceetgt ettgteeete egteeggeet ttetetgeet tteegteete etgeeteeee
1141 atotototot gotagtootg gtocagoogg accoccacoc acagtogggo cocagogott
1201 gageetgagt gtetgeteeg geeegtggag gtggagggag gggaegeeaa tgaeeteace
1261 agoccototo ogaccaccoo occotttoco ttttcaactt ttccaacttt toottoogtg
1321 ccctcctccg agcgcggcgg cgtgagccct gcaaggcagc cgctccgtct gaatggaaaa
1381 ggcaggcagg gagggtgagt caggatgtgt caggcegeec teceetgeeg cetgeeceec
1441 georgeorge eccageere tatataacce eccaggegte cacacteert cactgoogeg
1501 gecetgetge teagggeaca tgeeteeet ceceaggeeg eggeeeaget gaceeteggg
1561 geteccegg cageggacag ggaagggtta aaggeeeeeg getecetgee eeetgeeetg
1621 gggaacccct ggccctgtgg ggacatgaac tgtaagttgg ttcatgggga gggtggaggg
1681 gacagggagg cagggaggag agggacccac ggcgggggtg ggagcagacc ccgctgagtc
1741 gcacagagag ggacccggag acaggcagcc ggggaggaga gcagcttcgg agacaggagg
1801 cggcggagga gatgggcaga gagagacaca gacaggagcg gatggaggca gccaatcaga
1861 ggcgccgcag gagggacggg ccagacaggg ccccgagagg gagcgagacg cggagaccga
1921 gcagggcag ggacgcaggg actggtgccg ggagggaggt gacccccatc gacccaggcc
1981 ccagggagcc cgcggggacc gggagactcc ctgggattcc ggcagagagg ctccggaggg
2041 aaactgaggc agggtccgcg gagagcggag caagccaggg agtagcgacc ccagccgggg
2101 ggaggagaga gactgggcgc ggggggaaag cggggagagc cgggcagatg cggccgacgg
2161 aggcgcggac agaccgacgg ctggcgggcc cggggggcgg gctgggggtg tgcgaggcgc
2221 gggcggccgg ggagcgctga ttggctggcg ggtggccggg tgggcggggc ggccggggtg
2341 cagetetece getecegegg eceggeeggg eceatggete tgeceetete egeceaggtg
2401 cgctgcggcc cgggcttctg ccgcccaccc ggcggggctc ctgggagggc gtctaagggg
2461 tetecegtgg gagaggteeg tgteteeegg geteegteet ggettetgge teetteeeet
2521 geteccagee ageteggget ecegeggeee ggggaggggg caggttetgg cetgtgeete
2581 ccccaccatg ccccgccccg gggcccagat tccggcgtcc gggggcggac gggagacgcc
2641 eggecegtet accegeceg ggeegegtet geteegaegg geggggeage eagageeagg
2701 gagggagagg gaagcccgcc tggccctgcg acctgcccgc gggcgttcca ccctgggact
2761 taagacetee ageteeatee teectaagge egggagteea ggeeceagae eeteeteece
2821 gagacccagg agtccagacc ccaggccttc ctccctcaga cctaggagtc caggccccca
2881 geeteteete eeteagaeee aggaggagte eagaeeeeag tteeteetee eteagaeeeg
2941 ggagtccagg cccaggccct cctctctcag acccggagtc cagcctgagc tctctgcctt
3001 atcctgcccc caggtgtttg ccgcctggtc ctggtcgtgc tgagcctgtg gccagataca
3061 getgtegeee etgggeeace acetggeeee cetegagttt ecceagaeee tegggeegag
3121 ctggacagca ccgtgctcct gacccgctct ctcctggcgg acacgcggca gctggctgca
3181 cagctggtag gagagactgg gctggggcca gcacaggagt gagaggcaga gaggaacgga
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```
3241 gaggagtotg cgggcagcca cttggagggg ttctgggctc tcaggtggca gagtgaggga
3301 ggggaagagt tgggggcctg gcgtggggga tggagggagc cccgaggctg ggcaggggcc
3361 acctcacage tittitcect gecagagiga caaatteeca getgaegggg accacaacet
3421 ggattecetg eccaecetgg ceatgagtge gggggeactg ggagetetae aggtaaggge
3481 aagggagtgg gctggggaca aggtgggagg caggcagtga aggggggggg gaggatgagg
3541 ggcactggtc gggtgttctc tgatgtcccg gctctatccc cagctcccag gtgtgctgac
3601 aaggotgoga goggacotac tgtoctacot goggoacgtg cagtggotgo googggoagg
3661 tggctcttcc ctgaagaccc tggagcccga gctgggcacc ctgcaggccc gactggaccg
3721 getgetgege eggetgeage teetggtatg teetggeece aagacetgae acceeagace
3781 cocaccoctg gooccaaaat cotgtggcot gagtoottga agootgagao cocagaccog
3841 agtgcaacag ccccgetctg agaccctgac accctaacag cccgctctga gaccctgaca
3901 ccgtaacage cccgctctga gaccctgace ctaacagtee tgctctgaga ccctgaccct
3961 geagteceaa gateetgtgg ceetgagace etgaggeeet agaceeceaa ateetgeeea
4021 gaaacttcaa atteteacce aagaceetga gaeteeatea teeatgaeet caaagteece
4081 agateccage cectaagace caagacecca teetgaagee caaageettg agaatteaaa
4141 tecteacete aagaettgga gaeeetggee ecatgaeatt gaaaaceatg gaeetggeea
4201 ggcgtggtgg ctcacgcctg taatcccagc actttgggag gccgaggcaa gtggatcacc
4261 tgaggtcggg agttcaagac cagccagacc aacatggtga aaccctgtct ctactaaaaa
4321 tacaaaatta gccaggcgtg gtggtgcatg cctgtaatcc cagctacttg ggaggctgag
4381 gcaggagaat cgcttgaacc tgggaggcgg aggttgcagt gagccgagat cgcaccatta
4501 aaaagaagga aaagaaaacc atggacctcc agaccctgag accccaggcc ccagccctga
4561 gatectgaca tettaaagat eecaggeeet aagatacaag acettgacee aaageeagee
4621 ttgggaccct ggctgtacaa acccaagacc tccaggacct agaccccgag ccctgaggcc
4681 ctatgtetea eteceaacat egaaaaceet gacaceteag atectgagee tgegeetgta
4741 cgactccaag acceteaett ccaaagecag geecaaagee etgagaceag aagaetteaa
4801 accetggtte ttgggcetaa etceaaagae eetggatete aaatteeaae ttetagetet
4861 gagactecag coetcaccca tgagttectg aacttgaace cagagacece atetetaaga
4921 cttcagcctt gagatccagg gcctgaccct agactcgagc ccacagacct cagatactgt
4981 ctgtaaaacc ccagctctgg tggggagcag tggctcactc ctgtaatccc aaggcagggg
5041 aggccaaggc agaaggacet ettgaggeca tgagtttgag acageetggg cageatagea
5101 agactctgtt tcttaattat tattattatt attattttt ggagacagag tctcgcgctc
5161 tgttgcccag gctagagtgc aatggtgcca tttcggcttg ctggaacctc cgcctcctgg
5221 getcaagcga tteteetgee teageeteet gagtagetgg gaetteaggt geacactgee
5281 acacceggat aatttttttg tattttagta gacacagggt ttcaccgtgt tgcccagget
5341 gqtcacaaac toctgagctc aggccatccg cccgcctcgg cctcccaaag cgctgggata
5401 acaggegtga tecegegege etggettett aattgtteta acageageea caacaacaaa
5461 aacccagete tgagatteca geeeggega etetaacagt eecaggeeeg ateceteace
5521 tagaaccgag atgccagccc tgactccaca gacttcaccc ccaaccccca cactcagctc
5581 tggaagcccg tectgaetee ageeteeatt tteggaacce caeagcetga agageteeeg
5641 gectaaacae tteaceceae gegecacagt ceceetgtga atatgeagee eegatteage
5701 tgcagctcca cagcacccct gccctgcacc cccgctgcac cccctacctg tgactcacct
5761 ctctcctctc cccacagatg tecegeetgg ceetgeecca gecaceeegg gaceegeegg
5821 egecceget ggegeeece tecteageet gggggggeat cagggeegee caegecatee
5881 tgggggggct gningnictgaca cttnininitggg ccgtgagggg actgctgctg ctgaagactc
5941 ggctgtgacc cggggcccaa agccaccacc gtccttccaa agccagatct tatttattta
6001 tttatttcag tactgggggc gaaacagcca ggtgatcccc ccgccattat ctccccctag
6061 ttagagacag tccttccgtg aggcctgggg ggcatctgtg ccttatttat acttatttat
6121 ttcaggagca ggggtgggag gcaggtggac tcctgggtcc ccgaggagga ggggactggg
6181 gtcccggatt cttgggtctc caagaagtct gtccacagac ttctgccctg gctcttcccc
6241 atctaggect gggcaggaac atatattatt tatttaagca attactttte atgttggggt
6301 ggggacggag gggaaaggga agcctgggtt tttgtacaaa aatgtgagaa acctttgtga
6361 gacagagaac agggaattaa atgtgtcata catatccact tgagggcgat ttgtctgaga
 6421 gctggggctg gatgcttggg taactggggc agggcaggtg gaggggagac ctccattcag
 6481 gtggaggtcc cgagtgggcg gggcagcgac tgggagatgg gtcggtcacc cagacagctc
 6541 tgtggaggca gggtctgagc cttgcctggg gccccgcact gcatagggcc gtttgtttgt
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```
6601 tttttgagat ggagtetege tetgttgeet aggetggagt geagtgagge aatetaaggt
6661 cactgcaace tecaceteee gggtteaage aatteteetg ceteageete eegattaget
6721 gggatcacag gtgtgcacca ccatgcccag ctaattattt atttcttttg tatttttagt
6781 agagacaggg tttcaccatg ttggccaggc tggtttcgaa otcctgacct caggtgatcc
6841 tectgeeteg geeteecaaa gtgetgggat tacaggtgtg agceaccaca cetgacceat
6901 aggicticaa taaatattia atggaaggit ccacaagtca ccctgtgatc aacagtaccc
6961 gtatgggaca aagctgcaag gtcaagatgg ttcattatgg ctgtgttcac catagcaaac
7021 tggaaacaat ctagatatcc aacagtgagg gttaagcaac atggtgcatc tgtggataga
7081 acgccaccca gccgcccgga gcagggactg tcattcaggg aggctaagga gagaggcttg
7141 cttgggatat agaaagatat cctgacattg gccaggcatg gtggctcacg cctgtaatcc
7201 tggcactttg ggaggacgaa gcgagtggat cactgaagtc caagagtttg agaccggcct
7261 gcgagacatg gcaaaaccct gtctcaaaaa agaaagaatg atgtcctgac atgaaacagc
7321 aggetacaaa accaetgeat getgtgatee caattttgtg tttttettte tatatatgga
7381 ttaaaacaaa aatcctaaag ggaaatacgc caaaatgttg acaatgactg tetecaggte
7441 aaaggagaga ggtgggattg tgggtgactt ttaatgtgta tgattgtctg tattttacag
7501 aatttctgcc atgactgtgt attttgcatg acacatttta aaaataataa acactatttt
7561 tagaataaca gaatatcagc ctcctcctct ccaaaaataa gccctcagga ggggacaaag
7621 ttgaccgctg attgagcctg tcagggctgt gcactaagtg tgggcttttt acttacacaa
7681 tecteetgga etettgaata egecetgttt tacaggegag ggaaactgag tetcagacaa
7741 ggagtgggga ctctgttgca caaagtcaca cagctaggga gaggtggaag tgggattctg
7801 cgccgtgtct ggctctttcc caaagctctc tttgcaagtc ggtgttgagg aatcctcgcc
7861 acatgcacac acatgagata tggagaaaca ggttcagtaa ggatttgggt cttacccagg
7921 gcctagagaa gggtcaatgg cagagtaggg atgataattc aaatgcttta gttacttttc
7981 cctttacaat aacccagaca gacttccagg ggccccgtgt cgtcactagt ttgagtctgg 8041 ggttggaggt gcccatcctg ggcccggagt tttgattcac ccatcatagc cctcaagact
8101 ccaggetgge tgggcgcggt ggctcacgcc tgtaatccca gcactttggg aggctgaggc
8161 gggtggatca cttgaggtca ggagttcaag gccagcctga ccaacatgga gaaaccctgt
8221 ctctactaaa aatacaatcc agctactcgg aaggctgagg caggagaatc gctcgaaccc
8281 aggagacggg ggttgcggtg agccgagatc acatcacaaa cagccctagg cagtgcgggg
8341 ccccaggcga ggctcagacc tgcctccaca gagctgtctg ggtgatcgtg cctcctccgt
8401 ggaggcaggg tttgagcctc ccctgggggc cccgcactgc taaggctgtt tgtttttgcg
8461 atggagtete getetgttge etaggetgga gtgcagtgtg gcaatetaag etcactgeet
 8521 gggcaacaag agtgaaattc catctcaaaa aacaaaaaac aaacaaacaa acaaaaaact
 8581 ccaggetgta tecetggagg agaagggage ecacagteee eggagagtte etggaagagg
 8641 cccctgtgtg tccgatgagg tcacaaagcc cctccaccag aggetcetec cccagacccc
 8701 tgctgtccac cctggcaggg ccatggcgga ggcccgagtc tcccagcctg gggcatctcc
 8761 acgctctgta acgctgagct ccaggcaccc gtgaagcccc acgggtcaag gctggtgggc
 8821 cggggctggg aggcctgcac gcctgggttc tgggtcccta aaccagtacc catccaccac
 8881 agccaccatg atctggcttc gaaacaggag gtgccttgag ccgctccagg gcaccccgaa
 8941 gtgggtccct gttctggggg agctgcaaaa gaccctccag aagggcgagt acctgcccct
 9001 ccgtccgctg cccatgttcg agagtaactt tgttcaggtc tccagttccc agtgccccgg
 9061 ggctgagagg gacagagggg aagcaaggcc ccccgtgctg ggggatcttg agagggaacg
 9121 ggatttagca gtcactgtgt gggggacgat caggagggag gctcaggctg tggctgctgg
 9181 aggaaggagt ggtcccagcc ccctctccct ggctgcccca ggtgacccat caagggggcc
 9241 cagtgttcgt gaatcacaga accaaccggc tggccatggg cgtggccgcc tccctgccag
 9301 gcctggtgtt gcctgacatc ttgctgatcg gccagcccgc cgaggacagg gactgctccg
 9361 gcctcgtgct gaccaggtgc cgcatccccc aacccctcgg ccgccccctc cacccctcct
 9421 getetagacg etecectete ceteteceag gatgatecee etggaceteg tecacetetg
 9481 cgtccatgac ctctctgcct ggcgcctgaa gctgcgcctg gtctcgggcc gccagtacta
 9541 cctggccctg gacgcccctg acaacgaggt gggcttcctg ttccactgct gggtccgcct
 9601 catcaacctg cttcaggage cggetcecae etggaccece aggaccaege geacggeece
 9661 cctggatatg ccgctggcca aagcgcctgc ctccacctgg cacctgcagg tgggatccca
 9721 gctccacaga ccagggcatg gcaggcccca ggaaccctcc ggccagatcc agaggggact
 9781 cgaccaagag cccaaagtct agg
```

wherein the codon  $n_1n_2n_3$  and the codon  $n_4n_5n_6$  are as defined in Figure 16A.

//

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# mRNA of IL-11 mutein deriving from human IL-11 -SEQ ID NO:75-:

gaa ggg uua aag gee eec gge uee eug eec eeu gee eug ggg aac eec ugg eec ugu ggg gac aug aac ugu guu ugc cgc cug guc cug guc gug cug agc cug ugg cca gau aca gcu guc gcc ccu ggg cca cca ccu gge cce ccu ega guu uce cca gae ccu egg gee gag eug gae age ace gug eue eug ace cgc ucu cuc cug gcg gac acg cgg cag cug gcu gca cag cug agg gac aaa uuc cca gcu gac ggg gac cac aac cug gau uce cug ccc acc cug gcc aug agu gcg ggg gca cug gga gcu cua cag cuc cca ggu gug cug aca agg cug cga gcg gac cua cug ucc uac cug cgg cac gug cag ugg cug cgc cgg gea ggu gge ueu uec eug aag ace eug gag eec gag eug gge ace eug eag gee ega eug gae cgg cug cug cgc cgg cug cag cuc cug aug ucc cgc cug gcc cug ccc cag cca ccc ccg gac ccg ccg geg eee eeg eug geg eee eee uee uea gee ugg ggg gge auc agg gee gee eae gee auc eug ggg ggg cug  $n_1n_2n_3$  cug aca cuu  $n_4n_5n_6$  ugg gcc gug agg gga cug cug cug cug aag acu cgg cug uga ccc ggg gcc caa agc cac cac cgu ccu ucc aaa gcc aga ucu uau uua uuu auu uau uuc agu acu ggg gge gaa aca gee agg uga uee eee ege cau uau eue eee eua guu aga gae agu eeu uee gug agg ccu ggg ggg cau cug ugc cuu auu uau acu uau uua uuu cag gag cag ggg ugg gag gca ggu gga cuc cug ggu ccc cga gga gga ggg gac ugg ggu ccc gga uuc uug ggu cuc caa gaa guc ugu cca cag acu ucu gcc cug gcu cuu ccc cau cua ggc cug ggc agg aac aua uau uau uua uuu aag caa uua cuu uuc aug uug ggg ugg gga cgg agg gga aag gga agc cug ggu uuu ugu aca aaa aug uga gaa acc uuu gug aga cag aga aca ggg aau uaa aug ugu cau aca uau cca cuu gag ggc gau uug ucu gag agc ugg ggc ugg aug cuu ggg uaa cug ggg cag ggc agg ugg agg gga gac cuc cau uca ggu gga ggu ccc gag ugg gcg ggg cag cga cug gga gau ggg ucg guc acc cag aca gcu cug ugg agg cag ggu cug agc cuu gcc ugg ggc ccc gca cug cau agg gcc guu ugu uuu uuu gag aug gag ucu cgc ucu guu gcc uag gcu gga gug cag uga ggc aau cua agg uca cug caa ccu cca ccu ccc ggg uuc aag caa uuc ucc ugc cuc agc cuc ccg auu agc ugg gau cac agg ugu gca cca cca ugc cca gcu aau uau uua uuu cuu uug uau uuu uag uag aga cag ggu uuc acc aug uug gcc agg cug guu ucg aac ucc uga ccu cag gug auc cuc cug ccu cgg ccu ccc aaa gug cug gga uua cag gug uga gec acc aca ceu gac cea uag gue uuc aau aaa uau uua aug gaa ggu ucc aca agu cac ccu gug auc aac agu acc cgu aug gga caa gcu gca agg uca aga ugg uuc auu aug gcu gug uuc acc aua gca aac ugg aaa caa ucu aga uau cca aca gug agg guu aag caa cau ggu gca ucu gug

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gau aga acg cca ccc agc cgc ccg gag cag gga cug uca uuc agg gag gcu aag gag aga ggc uug cuu ggg aua uag aaa gau auc cug aca uug gcc agg cau ggu ggc uca cgc cug uaa ucc ugg cac uuu ggg agg acg aag cga gug gau cac uga agu cca aga guu uga gac cgg ccu gcg aga cau ggc aaa acc cug ucu caa aaa aga aag aau gau guc cug aca uga aac agc agg cua caa aac cac ugc aug cug uga ucc caa uuu ugu guu uuu cuu ucu aua uau gga uua aaa caa aaa ucc uaa agg gaa aua cgc caa aau guu gac agu ugu cuc cag guc aaa gga gag agg ugg gau ugu ggg uga cuu uua aug ugu aug auu guc ugu auu uua cag aau uuc ugc cau gac ugu gua uuu ugc aug aca cau uuu aaa aau aau aau aaa cac uau uuu uag aau

wherein the codon  $n_1n_2n_3$  and the codon  $n_4n_5n_6$  are both chosen among the group comprising the nucleotide codons which codes for a hydrophobic aminoacid, namely for Alanine (A), Valine (V), Leucine (L), Isoleucine (I), Phenylalanine (F), Methionine (M), Proline (P), Tryptophan (W).

 $n_1n_2n_3$  and  $n_4n_5n_6$  can be chosen among the group comprising the following nucleotide codons:

- GCU, GCC, GCA, GCG
- GUU, GUC, GUA, GUG,
- UUA, UUG, CUU, CUC, CUA, CUG,
- AUU, AUC, AUA,
- UUU, UUC,
- · AUG,
- CCU, CCC, CCA, CCG,
- UGG.

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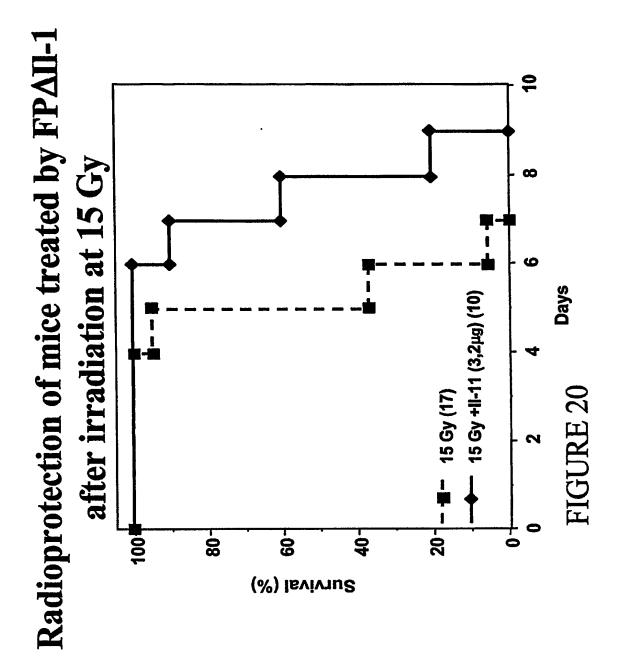
# Gene of IL-11 muteins deriving from human IL-11 – SEQ ID NO:76-:

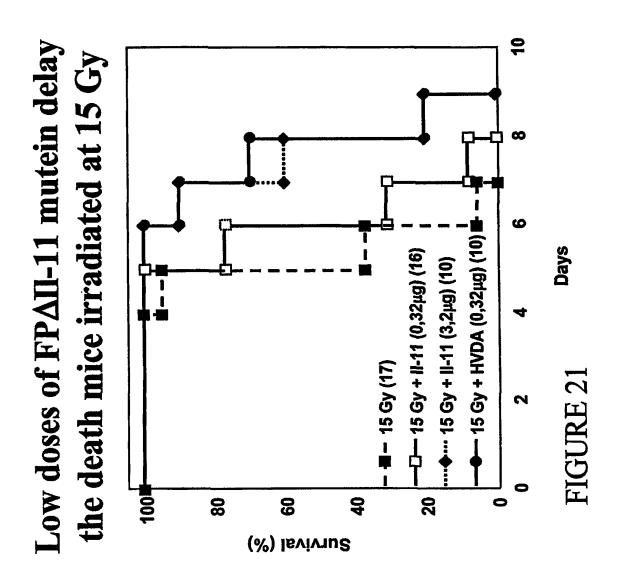
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ctgtaaaacc ccagctctgg tggggagcag tggctcactc ctgtaatccc aaggcagggg aggccaaggc agaaggacet ettgaggcca tgagtttgag acageetggg cagcatagca agactetgit tettaattat tattattatt attatttiti ggagacagag tetegegete tgttgcccag gctagagtgc aatggtgcca tttcggcttg ctggaacctc cgcctcctgg getcaagega tteteetgee teagesteet gagtagetgg gaetteaggt geacactgee acacceggat aattttttg tattttagta gaeacagggt tteacegtgt tgeecagget qqtcacaaac tcctgagctc aggccatccg cccgcctcgg cctcccaaag cgctgggata acaggegtga teeegegege etggettett aattgtteta acageageea caacaacaaa aacccaqctc tqaqattcca gccccggcga ctctaacagt cccaggcccg atccctcacc tagaaccgag atgccagccc tgactccaca gacttcaccc ccaaccccca cactcagetc tggaageeg teetgactee ageeteeatt tteggaacee cacageetga agageteeeg gcctaaacac ttcaccccac gcgccacagt ccccctgtga atatgcagcc ccgattcagc tgcageteca cageaccect gecetgeace eccgetgeac eccetacetg tgacteacet ctctcctctc cccacagatg tcccgcctgg ccctgcccca gccacccccg gacccgccgg egececeget ggegeeece teeteageet gggggggeat cagggeegee caegecatee tgggggggct gniningctgaca cttnininitggg ccgtgagggg actgctgctg ctgaagactc ggctgtgacc cggggcccaa agccaccacc gtccttccaa agccagatct tatttattta tttatttcag tactgggggc gaaacagcca ggtgatcccc ccgccattat ctccccctag ttagagacag teetteegtg aggeetgggg ggeatetgtg cettatttat aettatttat ttcaggagca ggggtgggag gcaggtggac tcctgggtcc ccgaggagga ggggactggg gtcccggatt cttgggtctc caagaagtct gtccacagac ttctgccctg gctcttcccc atctaggcct gggcaggaac atatattatt tatttaagca attacttttc atgttggggt qqqqacqqaq qqqaaaggga aqcctgggtt tttgtacaaa aatgtgagaa acctttgtga gacagagaac agggaattaa atgtgtcata catatccact tgagggcgat ttgtctgaga gctggggctg gatgcttggg taactggggc agggcaggtg gaggggagac ctccattcag gtggaggtee egagtgggeg gggeagegae tgggagatgg gteggteace eagacagete tgtggaggea gggtetgage ettgeetggg geceegeact geatagggee gtttgtttgt tttttgagat ggagtctcgc tctgttgcct aggctggagt gcagtgaggc aatctaaggt cactgcaacc tecacetece gggttcaage aatteteetg ceteageete eegattaget qqqatcacaq qtqtqcacca ccatqcccaq ctaattattt atttctttq tatttttaqt agagacaggg tttcaccatg ttggccaggc tggtttcgaa ctcctgacct caggtgatcc tectqcctcq qcctcccaaa gtgctgggat tacaggtgtg agccaccaca cctgacccat aggtottoaa taaatattta atggaaggtt coacaagtoa cootgtgato aacagtacco gtatgggaca aagctgcaag gtcaagatgg ttcattatgg ctgtgttcac catagcaaac tggaaacaat ctagatatcc aacagtgagg gttaagcaac atggtgcatc tgtggataga acqueacca geogeogga geagggactg teatteaggg aggetaagga gagaggettg cttgggatat agaaagatat cctgacattg gccaggcatg gtggctcacg cctgtaatcc tggcactttg ggaggacgaa gcgagtggat cactgaagtc caagagtttg agaccggcct qcqaqacatg gcaaaaccct gtctcaaaaa agaaagaatg atgtcctgac atgaaacagc aggetacaaa accactgeat getgtgatee caattttgtg tttttettte tatatatgga ttaaaacaaa aatcctaaag ggaaatacgc caaaatgttg acaatgactg tctccaggtc aaaggagaga ggtgggattg tgggtgactt ttaatgtgta tgattgtctg tattttacag aatttctgcc atgactgtgt attttgcatg acacatttta aaaataataa acactatttt tagaat

wherein the codon  $n_1n_2n_3$  and the codon  $n_4n_5n_6$  are as defined in Figure 16A.





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Parental (non-mutated) amino acid sequence of FPAIL-11 = SEQ ID NO:78 = MDYKDDDDKEGRRASVASPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPA DGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSS LKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRA AHAILGGLHLTLDWAVRGLLLLKTRL

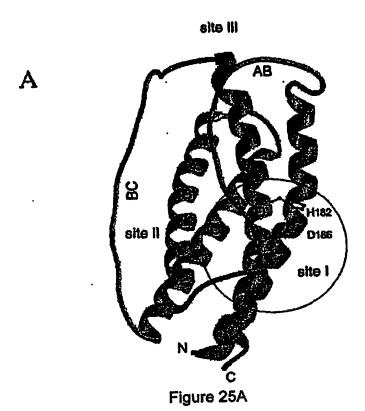
## 35/48

Mutated amino acid sequence of FPAIL-11 = SEQ ID NO:80 of the invention = MDYKDDDDKEGRRASVASPDPRAELDSTVLLTRSLLADTRQLAAQLRDKFPA DGDHNLDSLPTLAMSAGALGALQLPGVLTRLRADLLSYLRHVQWLRRAGGSS LKTLEPELGTLQARLDRLLRRLQLLMSRLALPQPPPDPPAPPLAPPSSAWGGIRA AHAILGGL<u>V</u>LTL<u>A</u>WAVRGLLLLKTRL

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# Primers used for inverse PCR mutagenesis of FPAIL-11:

Muteins	Primers
H182/V	G422 pACACTTGACTGGGCCGTACGGGGAC (s) SEQ ID NO:81
	G412 pCAGAACCAGCCCCCCAGGATGG (as) SEQ ID NO:82
D186/V	G410 pACACTTGTCTGGGCCGTACGGGGAC (s) SEQ ID NO:83
	G421 pCAGGTGCAGCCCCCCAGGATGG (as) SEQ ID NO:84
D186/A	G411 pACACTTGCCTGGGCCGTACGGGGAC (s) SEQ ID NO:85
	G421 pCAGGTGCAGCCCCCCAGGATGG (as) SEQ ID NO:86
H182/V-	G410 pACACTTGTCTGGGCCGTACGGGGAC (s) SEQ ID NO:87
D186/V	G412 pCAGAACCAGCCCCCCAGGATGG (as) SEQ ID NO:88
H182/V-	G411 pACACTTGCCTGGGCCGTACGGGGAC (s) SEQ ID NO:89
D186/A	G412 pCAGAACCAGCCCCCCAGGATGG (as) SEQ ID NO:90



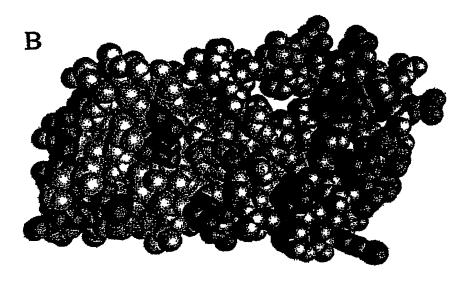


Figure 25B

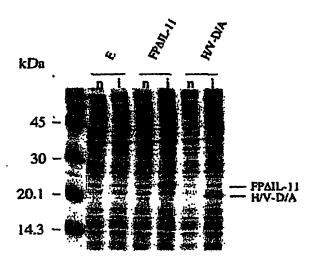


Figure 26

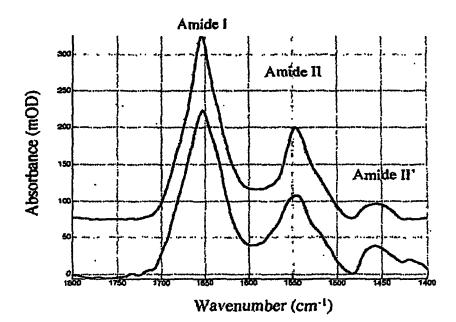


Figure 27

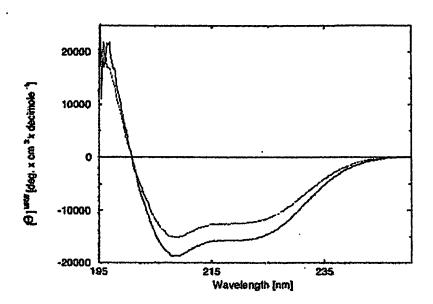


Figure 28

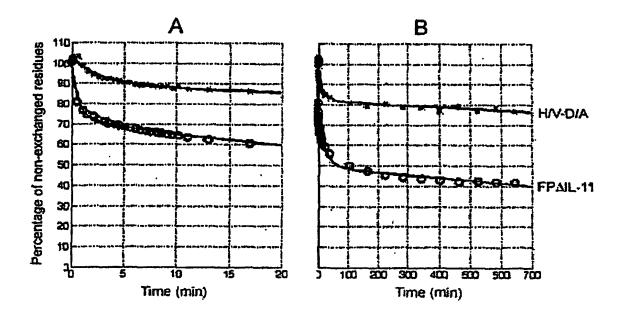
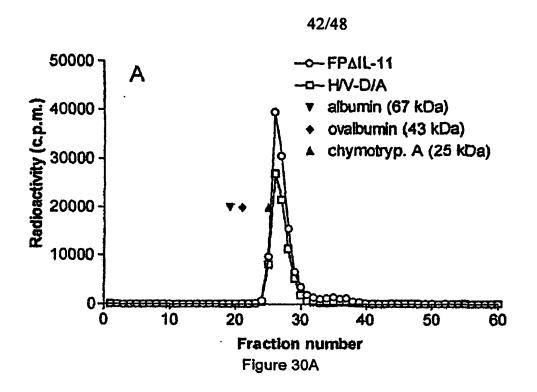


Figure 29A

Figure 29B



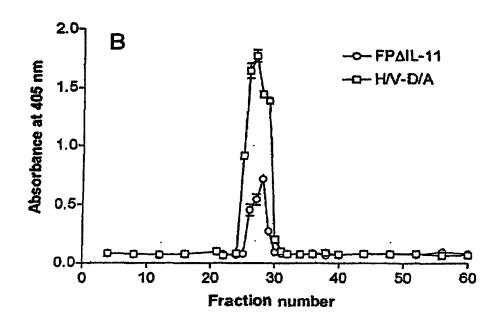
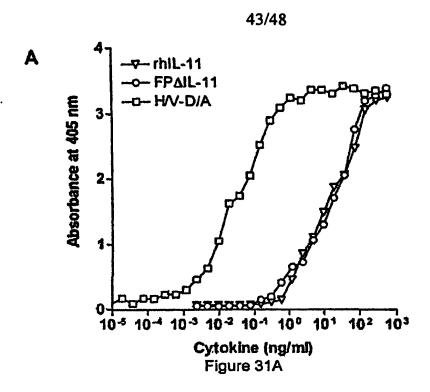


Figure 30B



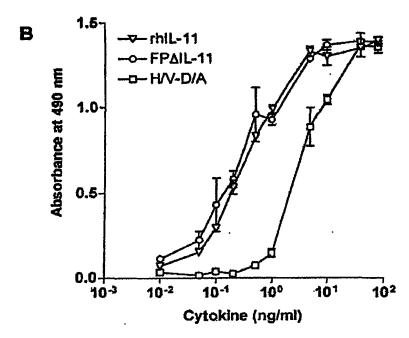


Figure 31B

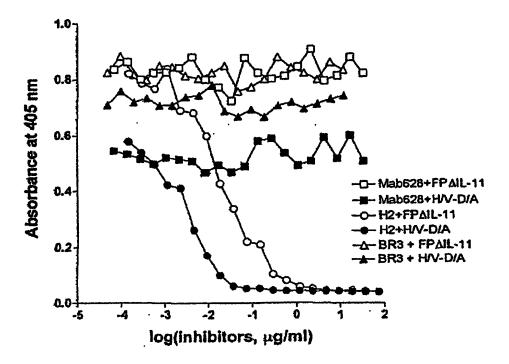


Figure 32

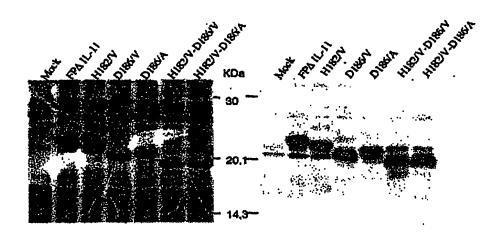


Figure 33

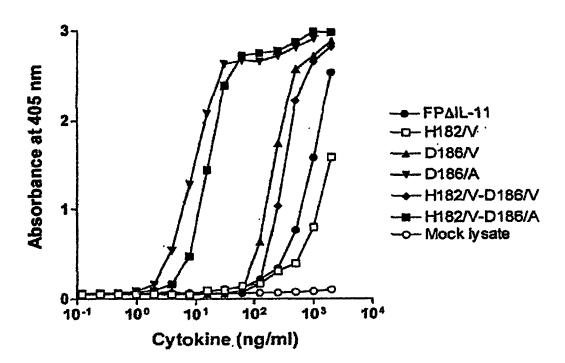


Figure 34

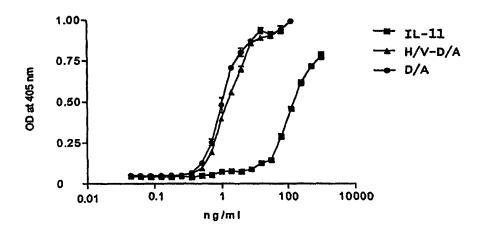


FIGURE 35

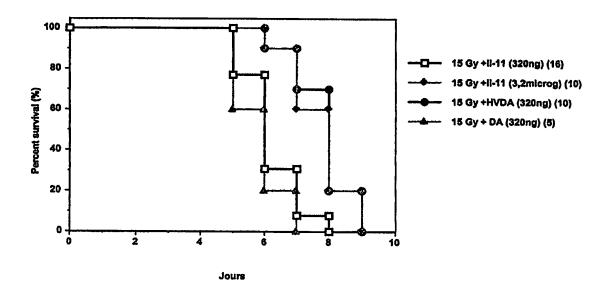


FIGURE 36